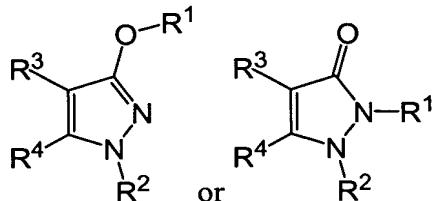


WHAT IS CLAIMED IS:

1. A compound of formula



5 or a pharmaceutically acceptable salt thereof, wherein

R¹ is H or C₁₋₈alkyl;

R² is C₁₋₈alkyl, phenyl, benzyl, R^c, R^f, C₁₋₄alkylR^c, C₁₋₄alkylR^f or R^g;

R³ is phenyl, naphthyl, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, 15 -S(=O)R^b, -S(=O)₂R^b, -S(=O)₂NR^aR^a, -S(=O)₂N(R^a)C(=O)R^b, -S(=O)₂N(R^a)C(=O)OR^b, -S(=O)₂N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)R^b, -N(R^a)S(=O)₂NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a;

R⁴ is phenyl, naphthyl, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, 20 -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b, -S(=O)₂R^b, -S(=O)₂NR^aR^a, -S(=O)₂N(R^a)C(=O)R^b, -S(=O)₂N(R^a)C(=O)OR^b, -S(=O)₂N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)R^b, 25 -N(R^a)S(=O)₂NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a;

R^a is independently at each instance H or R^b ;

R^b is independently at each instance C_{1-8} alkyl, phenyl or benzyl;

R^c is independently at each instance a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring

5 containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups;

R^d is independently at each instance C_{1-8} alkyl, C_{1-4} haloalkyl, halo, cyano,

10 nitro, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^aR^a$, $-C(=NR^a)NR^aR^a$, $-OR^a$, $-OC(=O)R^b$, $-OC(=O)NR^aR^a$, $-OC(=O)N(R^a)S(=O)_2R^b$, $-OC_{2-6}$ alkylNR^aR^a, $-OC_{2-6}$ alkylOR^a, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)_2NR^aR^a$, $-S(=O)_2N(R^a)C(=O)R^b$, $-S(=O)_2N(R^a)C(=O)OR^b$, $-S(=O)_2N(R^a)C(=O)NR^aR^a$, $-NR^aR^a$, $-N(R^a)C(=O)R^b$, $-N(R^a)C(=O)OR^b$, $-N(R^a)C(=O)NR^aR^a$, $-N(R^a)C(=NR^a)NR^aR^a$, $-N(R^a)S(=O)_2R^b$,

15 $-N(R^a)S(=O)_2NR^aR^a$, $-NR^aC_{2-6}$ alkylNR^aR^a or $-NR^aC_{2-6}$ alkylOR^a;

R^e is independently at each instance C_{1-6} alkyl substituted by 1, 2 or 3 substituents independently selected from R^d ;

R^f is independently at each instance R^c substituted by 1, 2 or 3 substituents independently selected from R^d ; and

20 R^g is independently at each instance R^b substituted by 1, 2 or 3 substituents independently selected from R^c , R^f and R^d .

2. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is H.

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3. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is C_{1-8} alkyl.

4. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R^2 is R^c , R^f , C_{1-4} alkylR^c, C_{1-4} alkylR^f or R^g .

5. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R² is C₁₋₈alkyl, phenyl or benzyl.

6. The compound of Claim 1 or a pharmaceutically acceptable salt
5 thereof, wherein R³ is phenyl or naphthyl both of which are substituted by 0, 1, 2 or 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b, -S(=O)R^b, -S(=O)NR^aR^a, -S(=O)N(R^a)C(=O)R^b, -S(=O)N(R^a)C(=O)OR^b,
10 -S(=O)N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)R^b, -N(R^a)S(=O)NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a.

7. The compound of Claim 1 or a pharmaceutically acceptable salt
15 thereof, wherein R³ is unsubstituted naphthyl or phenyl substituted by 1, 2 or 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b, -S(=O)R^b, -S(=O)NR^aR^a, -S(=O)N(R^a)C(=O)R^b, -S(=O)N(R^a)C(=O)OR^b,
20 -S(=O)N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)R^b, -N(R^a)S(=O)NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a.

8. The compound of Claim 1 or a pharmaceutically acceptable salt
25 thereof, wherein R³ is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)R^b,
30 -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b, -S(=O)R^b, -S(=O)NR^aR^a, -S(=O)N(R^a)C(=O)R^b, -S(=O)N(R^a)C(=O)OR^b, -S(=O)N(R^a)C(=O)NR^aR^a,

-NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a,
 -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)₂R^b, -N(R^a)S(=O)₂NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a
 or -NR^aC₂₋₆alkylOR^a.

5 9. The compound of Claim 1 or a pharmaceutically acceptable salt
 thereof, wherein R⁴ is a saturated or unsaturated 5- or 6-membered ring heterocycle
 containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the
 heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups
 and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or
 10 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b,
 -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a,
 -OC(=O)N(R^a)S(=O)₂R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b,
 -S(=O)₂R^b, -S(=O)₂NR^aR^a, -S(=O)₂N(R^a)C(=O)R^b, -S(=O)₂N(R^a)C(=O)OR^b,
 -S(=O)₂N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b,
 15 -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)₂R^b, -N(R^a)S(=O)₂NR^aR^a,
 -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a.

10. The compound of Claim 1 or a pharmaceutically acceptable salt
 thereof, wherein R⁴ is phenyl or naphthyl, both of which are substituted by 0, 1, 2 or
 20 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro, -C(=O)R^b,
 -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b, -OC(=O)NR^aR^a,
 -OC(=O)N(R^a)S(=O)₂R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a, -S(=O)R^b,
 -S(=O)₂R^b, -S(=O)₂NR^aR^a, -S(=O)₂N(R^a)C(=O)R^b, -S(=O)₂N(R^a)C(=O)OR^b,
 -S(=O)₂N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b, -N(R^a)C(=O)OR^b,
 25 -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)₂R^b, -N(R^a)S(=O)₂NR^aR^a,
 -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a.

11. The compound of Claim 1 or a pharmaceutically acceptable salt
 thereof, wherein R⁴ is pyridine or pyrimidine, both of which are substituted by 0, 1,
 30 2 or 3 substituents selected from C₁₋₈alkyl, C₁₋₄haloalkyl, halo, cyano, nitro,
 -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^aR^a, -C(=NR^a)NR^aR^a, -OR^a, -OC(=O)R^b,
 -OC(=O)NR^aR^a, -OC(=O)N(R^a)S(=O)₂R^b, -OC₂₋₆alkylNR^aR^a, -OC₂₋₆alkylOR^a, -SR^a,

-S(=O)R^b, -S(=O)₂R^b, -S(=O)₂NR^aR^a, -S(=O)₂N(R^a)C(=O)R^b,
-S(=O)₂N(R^a)C(=O)OR^b, -S(=O)₂N(R^a)C(=O)NR^aR^a, -NR^aR^a, -N(R^a)C(=O)R^b,
-N(R^a)C(=O)OR^b, -N(R^a)C(=O)NR^aR^a, -N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)₂R^b,
-N(R^a)S(=O)₂NR^aR^a, -NR^aC₂₋₆alkylNR^aR^a and -NR^aC₂₋₆alkylOR^a.

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12. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, provided that R⁴ is not pyridine or phenyl.

13. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is:

10 4-(4-chloro-phenyl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(4-chloro-phenyl)-1-piperidin-4-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(4-chloro-phenyl)-1-piperidin-3-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(4-chloro-phenyl)-1-piperidin-4-ylmethyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-
15 one;
4-(4-chloro-phenyl)-1-methyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(3, 4-dichlorophenyl)-1-piperidin-4-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(4-chlorophenyl)-1-(1-methyl-piperidin-4-yl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-
3-one;
20 4-(4-chlorophenyl)-1-(1-methyl-piperidin-3-yl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-
3-one;
4-(4-chlorophenyl)-1-(1-isopropyl-piperidin-4-yl)-5-pyridin-4-yl-1,2-dihydro-
pyrazol-3-one;
4-[4-(4-chlorophenyl)-3-methoxy-5-pyridin-4-yl-pyrazol-1-yl]-piperidine;
25 4-(3,4-dichloro-phenyl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(3,4-dichloro-phenyl)-1-isopropyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;
4-(3,4-dichloro-phenyl)-1-isopropyl-2-methyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-
one;
30 4-(3,4-dichloro-phenyl)-2-methyl-5-pyridin-4-yl-1-pyridin-3-ylmethyl-1,2-dihydro-
pyrazol-3-one;
1-cyclohexylmethyl-4-(3,4-dichloro-phenyl)-2-methyl-5-pyridin-4-yl-1,2-dihydro-
pyrazol-3-one;

1-(4-aminocyclohexyl)-4-(4-chlorophenyl)-5-pyridin-4-yl-1,2-dihdropyrazol-3-one;
1-(4-aminocyclohexyl)-4-naphthalen-2-yl-5-pyridin-4-yl-1,2-dihdropyrazol-3-one;
or
4-naphthalen-2-yl-1-(3-phenylpropyl)-5-pyridin-4-1,2-dihdropyrazol-3-one.

5

14. A pharmaceutical composition comprising a compound according to
Claim 1 and a pharmaceutically acceptable carrier or diluent.

10 15. A method of treatment of inflammation comprising administering an
effective amount of a compound according to Claim 1.

16. A method of treatment of rheumatoid arthritis, Pagets disease,
osteoporosis, multiple myeloma, uveitis, acute or chronic myelogenous leukemia,
pancreatic β cell destruction, osteoarthritis, rheumatoid spondylitis, gouty arthritis,
15 inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis,
Crohn's disease, allergic rhinitis, ulcerative colitis, anaphylaxis, contact dermatitis,
asthma, muscle degeneration, cachexia, Reiter's syndrome, type I diabetes, type II
diabetes, bone resorption diseases, graft vs. host reaction, Alzheimer's disease,
stroke, myocardial infarction, ischemia reperfusion injury, atherosclerosis, brain
20 trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock
syndrome, fever, myalgias due to HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV),
influenza, adenovirus, the herpes viruses or herpes zoster infection in a mammal
comprising administering an effective amount of a compound according to Claim 1.

25 17. A method of lowering plasma concentrations of either or both TNF- α
and IL-1 comprising administering an effective amount of a compound according to
Claim 1.

30 18. A method of lowering plasma concentrations of either or both IL-6 and
IL-8 comprising administering an effective amount of a compound according to
Claim 1.

19. A method of treatment of a pain disorder in a mammal comprising administering an effective amount of a compound according to Claim 1.

5 20. The manufacture of a medicament comprising an effective amount of a compound according to Claim 1.

21. The manufacture of a medicament for the treatment of inflammation comprising an effective amount of a compound according to Claim 1.

10 22. The manufacture of a medicament for the treatment of rheumatoid arthritis, Pagets disease, osteoporosis, multiple myeloma, uveitis, acute or chronic myelogenous leukemia, pancreatic β cell destruction, osteoarthritis, rheumatoid spondylitis, gouty arthritis, inflammatory bowel disease, adult respiratory distress syndrome (ARDS), psoriasis, Crohn's disease, allergic rhinitis, ulcerative colitis, 15 anaphylaxis, contact dermatitis, asthma, muscle degeneration, cachexia, Reiter's syndrome, type I diabetes, type II diabetes, bone resorption diseases, graft vs. host reaction, Alzheimer's disease, stroke, myocardial infarction, ischemia reperfusion injury, atherosclerosis, brain trauma, multiple sclerosis, cerebral malaria, sepsis, septic shock, toxic shock syndrome, fever, myalgias due to HIV-1, HIV-2, HIV-3, 20 cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses or herpes zoster infection in a mammal comprising an effective amount of a compound according to Claim 1.

25 23. A method of making a compound according to Claim 1, comprising the steps of:

reacting $R^3\text{-}CO_2H$ with $R^4\text{-}C(=O)H$ in the presence of trialkylamine and acetic anhydride;
protecting the resulting acid with a protecting group; and
reacting the protected acid with hydrazine to form

